Biochemistry

COMPARISON OF ELECTRON TRANSFER PROPERTIES OF FREE AND ANALOG BOUND MUTATED FORMS OF GLUTARYL COENZYME A DEHYDROGENASE

Paul R. Lentz[1], Gregory S. Furdek[1], Frank E. Frerman[+], and Colleen M. Byron[1]*
[1] Department of Chemistry, Ripon College, Ripon, WI 54971
[+] Department of Pediatrics, University of Colorado Health Sciences Center, Denver, CO 80262
lentzp@ripon.edu

This study investigates the spectroelectrochemical characteristics of the electron transfer properties of mutant forms of human Glutaryl Coenzyme A Dehydrogenase (GCD) using a uv-visible spectrophotometer and a potentiostat simultaneously. This enzyme, found in mammalian mitochondria, is the catalyst for the oxidative decarboxylation of glutaryl-CoA into crotonyl-CoA in the degradation of the amino acids tryptophan, lysine, and hydroxylysine. A deficiency of GCD in humans leads to a disease called Glutaric Aciduria (Acidemia) Type I, for which there is no known cure, leading to death at an early age. The particular mutants under study, E370Q and R94Q, represent amino acid substitutions involved in both catalysis and substrate binding. Our work focused primarily on the effects of the substrate analogs, 3-thiaglutaryl-CoA and 4-nitrobutyryl-CoA, on the midpoint potential of R94Q GCD. Complexation effects with 3-thiaglutaryl-CoA were similar to that seen with wild type GCD while 4-nitrobutyryl-CoA appears to shift the midpoint potential of R94Q GCD in a positive direction.